WASHINGTON STATE DEPARTMENT OF HEALTH
Office of Environmental Health Assessments

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SUBJECT: WASHINGTON STATE DEPARTMENT OF HEALTH'S EVALUATION OF EPA'S PERCHLORATE DRINKING WATER PRELIMINARY REMEDIATION GOAL (PRG).

Background:

Perchlorate was discovered by the U.S. Environmental Protection Agency (EPA) in private drinking water wells in a portion of the Deep Creek area of western Spokane County in early 2006. Since that discovery, EPA has sampled additional wells and continues to find perchlorate at low levels across the study area. The perchlorate levels range from non-detected to 3.2 micrograms per liter (ug/l). These levels are not considered an immediate health risk.

There are no federal or Washington State drinking water standards for perchlorate. However, EPA uses a 24.5 ug/l perchlorate drinking water equivalent level (DWEL)[1] as a preliminary remediation goal (PRG). EPA has taken no actions to date to reduce or eliminate perchlorate exposures in the Deep Creek area because the levels detected in drinking water wells do not exceed the EPA PRG. However, EPA's perchlorate PRG exceeds health protective levels set by various states, including Massachusetts where the drinking water standard is 2 ug/l. Because of these differences, EPA's Region 10 Emergency Response Unit requested that the Washington Department of Health (DOH) evaluate whether the EPA perchlorate PRG would be considered health protective for Washington citizens.

Animal and human studies have shown that perchlorate ingestion can decrease or inhibit iodide uptake, which can be a precursor to adverse health effects (hypothyroidism). DOH reviewed the

[1] EPA's Drinking Water Equivalent Level (DWEL) is a value derived by multiplying the reference dose (RfD) by typical adult body weight (70 kg) and dividing by daily water consumption (2 liters). The DWEL is normally multiplied by a percentage of the total daily exposure contributed by drinking water (often 20 percent) to determine a Maximum Contaminant Level Goal (MCLG) for contaminants in drinking water. EPA is using the perchlorate DWEL as a preliminary remediation goal.

most relevant of these perchlorate studies along with the perchlorate reference dose (RfD) work completed by EPA and National Academy of Science (NAS). DOH also reviewed perchlorate evaluations completed by Massachusetts and California, two states where significant work has been completed to develop perchlorate drinking water standards.

Health Studies and EPA Reference Dose Development

EPA completed its draft toxicological review of perchlorate in 2002, and proposed a reference dose (RfD) of 0.00003 milligrams per kilogram per day (mg/kg/day) based primarily on studies that identified neurodevelopmental deficits in rat pups. These deficits were linked to maternal exposure to perchlorate. Subsequently, NAS reviewed the health implications of perchlorate, and in 2005 proposed an alternative reference dose of 0.0007 mg/kg/day based primarily on the Greer et al, 2002 study. During that study, 37 human subjects were split into four exposure groups exposed to 0.007 (7 subjects), 0.02 (10 subjects), 0.1 (10 subjects), and 0.5 (10 subjects) mg/kg/day. Significant decreases in iodide uptake were found in the three highest exposure groups. Iodide uptake was not significantly reduced in the lowest exposed group, but four of the seven subjects in this group experienced inhibited iodide uptake. The RfD proposed by NAS was accepted by EPA and added to its integrated risk information system (IRIS) in 2005.

Much debate was generated following EPA's posting of the perchlorate RfD in 2005, most notably in commentary submitted to the journal Environmental Health Perspectives (EHP) by Ginsberg and Rice. The authors argued that the RfD was not adequately protective of human health for the following reasons:

1) The NAS report described the level of lowest exposure from Greer et al as a no observed effect level (NOEL). However, there was actually an effect at that level although not statistically significant largely due to small size of study population (four of seven subjects showed a slight decrease in iodide uptake).

2) Reduced iodide uptake was not considered to be an adverse effect. However, it is s a precursor to an adverse effect (hypothyroidism). Therefore, additional safety factors are necessary when extrapolating from the point of departure to the RfD.

3) Consideration of data uncertainty was insufficient because the Greer, et al study reflected only a 14-day exposure to healthy adults and no additional safety factors were considered to protect sensitive subpopulations. For example, the potential for greater toxicity to breastfeeding newborns was not considered

Blount, et al. evaluated 2001-2002 biomonitoring results from the National Health and Nutrition Examination Survey (NHANES) looking at urinary perchlorate, urinary iodine, and thyroid hormone levels and determined that total thyroxine (T4) and thyroid stimulating hormone (TSH) levels were related to urinary perchlorate in women. TSH and T4 levels were used as indicators of how well the thyroid was functioning. TSH causes the thyroid gland to produce triiodothyronine (T3) and T4. Both hormones are needed for normal brain development. Perchlorate was a significant positive predictor of TSH in women with urinary iodine >100 ug/l and significant positive predictor of TSH and negative predictor of T4 in women with low

urinary iodine (< 100 ug/l). This implies that women and fetuses of women with low dietary intake of iodine can be impacted by perchlorate at current exposure levels in the U.S. population. This is especially of concern because recent NHANES data show that nearly 17% of reproductive aged women in the U.S. have urinary iodine levels less than 50 ug/l. The World Health Organization classifies someone as being iodine deficient at a urinary iodine level less than 100 ug/l.

DOH Findings

To date, agencies have relied on the Greer, et al study as the critical study for deriving the RfD. However, Ginsberg, et al (2007) recently suggested further study should be conducted and incorporated into future risk assessments for developing perchlorate RfDs because of the findings by Blount, et al regarding thyroid hormone iodine levels in adult women.

Although there has generally been consensus with the critical study, there isn't consensus with regard to developing a perchlorate RfD. One of the key differences results from how the point of departure is viewed (i.e., NOEL or LOAEL), or whether a benchmark dose should be used to derive the RfD. Defining the point of departure as a NOEL or LOAEL has implications when it comes to applying appropriate safety factors to the point of departure to derive the RfD.

There also has not been consensus about setting PRGs and drinking water maximum contaminant levels (MCLs) (see CA and MA MCLs described below). An MCL is a legally enforceable standard for drinking water established under the Safe Drinking Water Act and is defined as the level above the maximum contaminant level goal (MCLG) that may be achieved with the use of the best available technology, treatment techniques, and other means which EPA finds are available taking cost into consideration. The MCLG is the maximum level of a contaminant in drinking water at which no known or anticipated adverse effect on the health of persons would occur, and which allows an adequate margin of safety.

MCLGs are generally derived using a DWEL multiplied by a source fraction of 20% (0.2).

$$\mathbf{MCLG = \frac{RfD \times BW \times SF}{IR}}$$

Where:

MCLG = Maximum Contaminant Level Goal
BW = Body Weight
RfD = Reference Dose
SF = Source Fraction (fraction of chemical exposure that comes from drinking water)
IR = Water Ingestion Rate

Using the standard EPA methodology and assumptions, the MCLG for perchlorate is approximately 5 µg/L.

Table 1 shows how Massachusetts and California derived their respective MCLs in relation to EPA's PRG. Each entity derived different values based on different assumptions. The key

assumptions responsible for these differences are the RfD and the source fraction. All entities derived different RfDs, and Massachusetts and California applied a source fraction acknowledging that drinking water is not the only source of perchlorate exposure. Data from U.S. Food and Drug Administration (FDA) show measurable levels of perchlorate in some foods.

Table 1. Comparison between EPA's derivation of the PRG and Massachusetts' and California's derivation of MCLs.

	EPA		**Massachusetts**		**California**	
Point of Departure (mg/kg/day)	NOEL		LOAEL		BMDL (5% reduction in mean thyroidal iodide uptake)	
	0.007		0.007		0.0037	
Uncertainty Factors	10	inter-individual variability	30	10 inter-individual variability x 3 use of LOAEL)	10	inter-individual variability
Reference dose (mg/kg/day)	0.0007		0.00023		0.00037	
Ingestion Rate (L/day)	2		2		NA	
Body Weight (kg)	70		70		NA	
Ratio Body weight : Ingestion Rate (kg/L/day)	35		35		25.2*	
Source Fraction (factor accounts for percent of perchlorate exposure from drinking water)	1		0.2		0.6	
Concentration (mg/L)	0.0245		0.0016		0.0056	
PRG or MCL (ug/L)	24.5 (PRG)		2 (MCL)		6 (proposed MCL)**	

*Body weight to water consumption rate ratio for the 95th percentile of the pregnant woman population.
** California Department of Health Services proposed the MCL in September 2006. The proposed MCL is currently going through the rulemaking process.
NOEL – No observed effect level
LOAEL – Lowest observed adverse effect level
BMDL – Benchmark Dose (lower confidence limit)

In addition to the different MCLs and the PRG presented above, recent analysis suggests that the PRG developed by EPA should be improved by considering infant exposures through breast-feeding (Ginsberg et al 2007). Maternal exposure to perchlorate at 24.5 ug/l in drinking water could lead to 90% of nursing infants with exposure in excess of the current RfD.

Based on a review of existing literature, DOH has identified the following concerns with EPA's perchlorate PRG:

- EPA's reference dose (RfD), which is the basis for the PRG, may not be protective of public health with a reasonable margin of safety.

- EPA's PRG only accounts for exposure through drinking water. Drinking water may only be a partial source of perchlorate exposure. Some consideration of potential dietary sources is necessary to be protective of human health particularly since the FDA has found perchlorate in some U.S. foods. According to EPA guidance for setting safe drinking water standards, DWELs, which in this case is equal to the perchlorate PRG, are normally multiplied by a source fraction for determining an MCLG. EPA typically uses a source fraction of 0.2 when little is known about other sources of exposure. As noted, use of the perchlorate DWEL established by EPA would approximate an MCLG of 5 µg/L, which is within the range of MCLs established by Massachusetts and California.

- Roughly 17% of reproductive-aged women in the U.S. are especially susceptible to perchlorate toxicity due to inadequate dietary intake of iodine. EPA's PRG may not be protective of women and fetuses of women who do not consume enough iodine.

- Nursing infants may be excessively exposed to perchlorate if mother is exposed to perchlorate in drinking water at the 24.5 ug/l PRG.

Because there is uncertainty regarding our understanding of perchlorate toxicity, exposure, and presence in the environment, a cautious approach for protecting sensitive populations should be taken. DOH concludes that EPA's PRG is not adequately protective of the health of sensitive subpopulations in Washington State.

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